September 23, 2008

Nature News

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MONOCLONAL ANTIBODIES COME OF AGE

A fast way of isolating antibodies from people has been used to create a library of the immune proteins produced by someone inoculated with a nicotine-acting vaccine. Roger Beerli and his team at Cytos Biotechnology in Schlieren, Switzerland, used lymphocytes from an individual who was enrolled in a clinical trial of the smoking-cessation vaccine, and with their technique rapidly identified nicotine-specific antibodies1 .

The work is the latest offering in a burgeoning field of therapeutics: monoclonal antibodies. These antibodies are derived from a single population of cells and bind to their target at a specific site. Last month, researchers reported that they had isolated functional antibodies from survivors of the 1918 influenza pandemic[2], and in April, another team reported the rapid cloning of influenza antibodies from people who had recently been vaccinated against the disease[3]. Researchers hope the findings will eventually lead to 'passive immunity' treatments.

The market for monoclonal antibodies is the fastest-growing segment of the pharmaceutical industry. In 2007, therapeutic monoclonal antibodies brought in more than US$26 billion, most of which came from treatments for cancer and autoimmune diseases. That same year, 50 companies had anticancer antibodies in clinical trials worldwide[4].

“Infectious-disease research has come full circle.”

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Genentech

The field has come a long way since pre-antibiotic days when infected patients were injected with a serum of horse antibodies from an animal that had been exposed to the same disease. Such treatments carried a high risk of serum sickness caused by immune reactions to the horse proteins. When small-molecule antibiotics emerged on the scene, animal serum therapies were largely abandoned.

Recent advances in antibody harvesting are breathing new life into the idea of passive-immunity therapy, this time with human antibodies. "Infectious-disease research has come full circle," says Andrew Chan, senior vice-president of immunology and antibody engineering at Genentech, a biotechnology company in South San Francisco, California.

The fundamental techniques for making monoclonal antibodies were laid down years ago, but as the market for monoclonal antibodies grows, companies are

modifying those techniques to overcome technical difficulties and to establish a hold in a crowded patent landscape. "Small biotechnology companies are trying to figure out new ways to work around existing intellectual property," says immunologist James Crowe of Vanderbilt University Medical Center in Nashville, Tennessee. "That gives them a high incentive to be innovative."

Isolating antibodies from immunized humans has its limits, however. "The key is that you have to start with a disease that you can immunize people against," says Crowe. Researchers cannot, for example, immunize patients against cancer or infectious diseases for which there is no approved vaccine. And, Crowe adds, "You're not going to immunize someone against the 1918 flu". However, people who were exposed to it but survived because of their own natural antibody response might have antibodies effective against future, similar strains. Other researchers have isolated antibodies from survivors of H5N1 avian flu[5].

In theory, such antibodies could be tested for use as therapies, but antibodies are much more difficult and expensive to produce than small molecules. At present, there is only one available targeted antibody therapy against an infectious disease — MedImmune's palivizumab, used to fend off respiratory syncytial virus in premature infants. Palivizumab brings in more than a billion dollars a year for the biotech company, based in Gaithersburg, Maryland, but few other infectious diseases are expected to be so lucrative.

The high specificity of an antibody is a valued asset in the clinic, but can be detrimental in the fast-changing world of infectious disease, in which viruses such as HIV can mutate out of an antibody's grasp. "We're seeing a little bit of rediscovering large molecules like monoclonal antibodies for infectious diseases," says Chan. "But it's still quite limited."

Some companies may be wary of trialling monoclonal antibody therapies after a trial in 2006 by the now-defunct German company TeGenero in which six healthy volunteers were left fighting for their lives. But the drug (TGN1412) the six took was unusual in that it activated immune cells rather than inhibiting them.

Human-produced antibodies could also be used as a research tool, says Antonio Lanzavecchia of the Institut e for Research in Biomedicine in Bellinzona, Swizerland. "I really believe this approach is going to be the major pathway to new vaccines," he says.